

INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

08 JUN 2005



Applicant's or agent's file reference F-12643/PCT-SS	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/IL 03/01057	International filing date (day/month/year) 11.12.2003	Priority date (day/month/year) 12.12.2002
International Patent Classification (IPC) or both national classification and IPC C07K14/47		
Applicant TEL AVIV UNIVERSITY FUTURE TECHNOLOGY ... et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

 These annexes consist of a total of 25 sheets.

3. This report contains indications relating to the following items:
 - I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

Date of submission of the demand 30.06.2004	Date of completion of this report 20.01.2005
Name and mailing address of the International preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Pinheiro Vieira, E Telephone No. +49 89 2399-7865 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/IL 03/01057

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-66 as originally filed

Claims, Numbers

1-166 as originally filed

177 received on 20.12.2004 with letter of 17.12.2004

Drawings, Sheets

1/6-6/6 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/IL 03/01057

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

see separate sheet

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☐ claims Nos.

because:

- ☒ the said international application, or the said claims Nos. 88-162 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-166,177
Inventive step (IS)	Yes: Claims	
	No: Claims	1-166,177
Industrial applicability (IA)	Yes: Claims	1-87,163-166,177
	No: Claims	88-162

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/IL 03/01057

2. Citations and explanations

see separate sheet

I. Basis

- I.1** The amendments filed with the letter dated 17.12.2004 introduce subject-matter which extends beyond the content of the application as filed, contrary to Article 34(2)(b) PCT. The amendments concerned are the following:
In claim 1 was introduced the expression "wherein the hydrophobic moiety...with better (l) membrane permeability **and/or** (b) interaction...patch of the GSK-3". It should be noted that page 26 last paragraph and page 27 first paragraph rather state "high inhibitory activity of the conjugates...derived from **both, the replacement... and the incorporation** of the hydrophobic moiety/moieties, which provides for a better membrane permeability ...**as well as** for a better interaction...".
At pages 7, 14, 15 and 23 of the description and claims 10, 41, 58, 83, 113, 123, 137, 144 and 158 the term **X3** has been replaced by **Y3**. The Applicant should know that the priority document does not serve as basis for amendments.
Claims 5, 36, 53, 78, 108, 132, 153 the expression "at least one" has been substituted by "at least five". Nowhere in the description could be found a basis for said amendment. The same objection applies to the new claims 167-176.
Claim 178 has no basis on the application as originally filed.

III. Non-establishment of Opinion.

- III.1** Independent claims 88, 118 and 142 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims and related dependent claims (Article 34(4)(a)(I) PCT).
The patentability can also be dependent upon the formulation of the claims. The EPO, for example, **does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment**, but may allow, however, claims to **a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment**.
The reformulation of independent claims 88, 118 and 142 and new dependent claims 175 and 176 do not fall within any of these formulations.

V. Reasoned statement.

This international preliminary examination report is drafted as if the amendments haven't been done except for claim 177 (see item I above).

V.1 Reference is made to the following documents:

- D1: WO 01/49709 A (ELDAR FINKLEMAN HAGIT ;UNIV RAMOT (IL); MCINNIS PATRICIA A (US)) 12 July 2001 (2001-07-12)
- D2: WO 02/24941 A (UNIV DUNDEE ;BIONDI RICARDO (GB); FRAME SHEELAGH (GB)) 28 March 2002 (2002-03-28)
- D3: OELRICHS P B ET AL: 'UNIQUE TOXIC PEPTIDES ISOLATED FROM SAWFLY LARVAE IN THREE CONTINENTS' TOXICON, ELMSFORD, NY, US, vol. 37, no. 3, 1999, pages 537-544, XP000994829 ISSN: 0041-0101
- D4: ELDAR-FINKELMAN H ET AL: 'The insulin mimetic action of glycogen synthase kinase-3 inhibitors' DIABETOLOGIA, vol. 45, no. Supplement 2, August 2002 (2002-08), page A 70 XP009031166 38th Annual Meeting of the European Association for the Study of Diabetes (EASD);Budapest, Hungary; September 01-05, 2002 ISSN: 0012-186X
- D5: PLOTKIN BATYA ET AL: 'Insulin mimetic action of synthetic phosphorylated peptide inhibitors of glycogen synthase kinase-3.' JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, vol. 305, no. 3, June 2003 (2003-06), pages 974-980, XP009031218 ISSN: 0022-3565

D1 and D2 disclose compounds with the sequence motif ZXXXS(p) which inhibit GSK3.

D2 discloses compounds with the sequence motif ZXXXS(p) which inhibit GSK3.

D3 discloses a peptide comprising the sequence ZXXXS(p).

D4 suggests the inhibition of GSK3 by a novel class of peptides. In view of D5, which is a post publication of the present abstract it appears that peptides with SEQ ID No16 were known at the present priority date of 12.12.02.

V.2 Novelty, inventive step and industrial applicability (Art. 33 PCT).

- 2.1 The present invention concerns conjugates for inhibiting Glycogen Synthase Kinase 3 (GSK3) comprising a) the a sequence comprising the motif ZX1X2X3S(p) where Z is any amino acid except serine or threonine (preferably alanine) and b) an hydrophobic moiety (can be a peptide sequence of minimum 1 amino acid (!) or a fatty acid) attached to the C- or N-terminus of the peptide.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/IL 03/01057

- 2.3 In view of the prior art documents D1-D4 the subject matter in claims 1-166 and 177 is neither novel nor inventive.
It should be noted that it is obvious that hydrophobic amino acid sequences attached to a functional domain can provide molecules with increased membrane permeability.
- 2.4 The subject matter in claims 88-162 is not industrial applicable (Art. 33(4) PCT).
- V.3** In view of the disclosure in the examples it appears that the peptide defined by SEQ ID No 16 bound to myristic acid would be inventive if document D4 is proved to be irrelevant.